UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/071,174	02/07/2002	John C. Reed	8014-014 US	2991

32301 7590 03/07/2006

CATALYST LAW GROUP, APC
9710 SCRANTON ROAD, SUITE S-170
SAN DIEGO, CA 92121

EXAMINER	
ANGELL, JON E	

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 03/07/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/071,174	REED ET AL.	
	Examiner	Art Unit	
	Jon Eric Angell	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 December 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4-28,76,77 and 142-163* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4-23,26-28,76,77 and 142-163* is/are rejected.

7)☒ Claim(s) *24 and 25* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *07 February 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on December 12, 2005 has been entered.

Claims 1, 4-28, 76, 77, 142-163 are currently pending in the application and are addressed herein.

Applicant's arguments are addressed on a per section basis. The text of those sections of Title 35, U.S. Code not included in this Action can be found in a prior Office Action. Any rejections not reiterated in this action have been withdrawn as being obviated by the amendment of the claims and/or applicant's arguments.

Claim Rejections - 35 USC § 112, 2nd paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 4-14, 26-28, 142-163 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The instant claims are indefinite because claim 1 is drawn to an isolated nucleic acid that comprises a sequence that is 95% or more identical to SEQ ID NO: 1 wherein the sequence is

distinct from SEQ ID NO: 37. Since SEQ ID NO: 1 is 887 nucleotides long and SEQ ID NO: 37 is 130 nucleotides long, any nucleic acid sequence that comprises a sequence that is 95% or more identical to SEQ ID NO: 1 would necessarily be distinct from the 130 nucleotide sequence of SEQ ID NO: 37. Therefore the limitation "wherein the sequence is distinct from... (SEQ ID NO: 37)" renders the claim indefinite because the claim, as written, does not encompass the sequence that is SEQ ID NO: 37, thus bringing into question why the limitation is included in the claim. Should Applicants intend to claim a sequence that is 95% or more identical to a sequence of SEQ ID NO: 1 (such as a fragment or variant fragment of SEQ ID NO: 1) wherein the sequence is not the nucleotide sequence of SEQ ID NO: 37, they should amend the claim to read as such.

It is noted that deleting the language "wherein the sequence is distinct from... (SEQ ID NO: 37)" would obviate this rejection.

Furthermore, claim 11, compounds the problem of claim 1 by reading on the isolated nucleic acid of claim 1 wherein the sequence is selected from, "(d) subsequences of either a, b, or c that are at least 25 base pairs long". As indicated above, since SEQ ID NO: 1 is 887 nucleotides long, any nucleic acid sequence that comprises a sequence that is 95% or more identical to SEQ ID NO: 1 would necessarily be at least 842 nucleotides long (95% of 887=842.65). Therefore the limitation "at least 25 base pairs long" renders the claim indefinite because the claim, as written, does not encompass sequences less than 95% identical to SEQ ID NO: 1 thus bringing into question why the limitation "at least 25 base pairs" is included in the claim. Should Applicants wish the claims to encompass nucleotides that are at least 25 base

pairs long, they should consider amending claim 1 such that it would encompass these sequences.

Additionally, claim 26 recites the limitation "**A** nucleic acid of claim 1" i.e., any nucleic acid of claim 1. There is insufficient antecedent basis for this limitation in the claim because claim 1 is drawn to "an isolated nucleic acid" (i.e. a single nucleic acid). Amending claim 26 to read "**The** nucleic acid of claim 1" would obviate this rejection.

Claim 142 recites the new limitation "the polypeptide" in line 6. There is insufficient antecedent basis for this limitation in the claim.

Claims 4-14, 27, 28 and 143-163 are included in the instant rejection because they are dependent claims

Claim Rejections - 35 USC § 112, 1st paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 17-23, 76 and 77 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 17-23 encompass sequences that are 95% or more identical to SEQ ID NO: 1; however, the claims do not indicate that the sequence encodes a polypeptide with a specific

function. Therefore, the claims encompass variants of SEQ ID NO: 1, that although they are at least 95% identical to SEQ ID NO: 1 they may encode non-functional variants or variants with a completely different function.

Claims 76-77 encompass nucleic acid sequences that encode polypeptides that are at least 65% identical to SEQ ID NO: 2; however, the claims do not indicate that encoded polypeptide has any specific function. Therefore, the claims encompass variants of SEQ ID NO: 2, that although they are at least 65% identical to SEQ ID NO: 2 they may encode non-functional variants or variants with a completely different function.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of compete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only distinguishing characteristic of the genus of molecules encompassed by claims 17-23 is that the sequence is 95% identical to SEQ ID NO: 1, and the only distinguishing characteristic of the genus of molecules encompassed by claims 76 and 77 is that the sequence encodes a polypeptide that is at least 65% identical to SEQ ID NO: 2. The claims do not identify any particular portion or critical elements of the nucleic acid molecule that must be conserved. Accordingly, the specification does not provide adequate written description of the claimed genus.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry,

whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of molecules, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

It is noted that, for claims 17-23, only isolated nucleic acids that are 95% or more identical to SEQ ID NO: 1 and which encode a polypeptide that inhibits apoptosis meet the written description provision of 35 U.S.C. §112, first paragraph. It is also noted that, for claims 76 and 77, only isolated nucleic acids that encode proteins that are 90% or more identical to SEQ ID NO: 2 and which inhibit apoptosis meet the written description provision of 35 U.S.C. §112, first paragraph Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Additionally, Claims 76, 77 162 and 163 rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for producing a polypeptide in solution or in vitro, does not reasonably provide enablement for a method of producing a polypeptide in vivo. The specification does not enable any person skilled in the art to which it

pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 112, first paragraph, have been described by the court in *In re Wands*, 8 USPQ2d 1400 (CA FC 1988).

> *Wands* states on page 1404,
> "Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims."

The nature of the invention

The claims encompass making a polypeptide in vivo and encompasses making the polypeptide as a therapeutic polypeptide in vivo, which encompasses gene therapy. As such, the invention is in a class of invention which the CAFC has characterized as "the unpredictable arts such as chemistry and biology." Mycogen Plant Sci., Inc. v. Monsanto Co., 243 F.3d 1316, 1330 (Fed. Cir. 2001).

The breadth of the claims

The instant claims are broad in the sense that the claims merely recite a method of producing a polypeptide comprising expressing a nucleic acid encoding an amino acid sequence... wherein the nucleic acid is expressed *in vivo*. Given their broadest reasonable interpretation consistent with the specification, the claims encompass expressing the polypeptide in order to treat a disease.

The unpredictability of the art and the state of the prior art

The specification does not disclose that the methods have effectively treated any disease or disorder by administering a nucleic acid which encodes the protein and expressing the protein *in vivo* in order to obtain a therapeutic effect.

It is noted that the claims are not directed to the treatment of any particular disease; therefore, given the broadest reasonable interpretation, the claims encompass treating any disease or disorder.

At the time of filing, the relevant art considered gene therapy as a whole to be unpredictable. For instance, **Anderson** (Nature 1998; 392(suppl):25-30) teaches,

> "The challenge is to develop gene therapy as an efficient and safe drug delivery system. The goal is more difficult to achieve than many investigators had predicted... The human body has spent many thousands of years learning to protect itself from the onslaught of environmental hazards, including the incorporation of foreign DNA into its genome. (See p. 25, second paragraph). The ultimate goal of gene therapy research is the development of vectors that can be injected, will target specific cells, will result in safe and efficient gene transfer into a high percentage of those cells, will insert themselves into appropriate regions of the genome (or will persist as stable episomes), will be regulated be either by administered agents or by the body's own physiological signals, will be cost effective and will cure disease. (See p. 30, first paragraph)."

Dang et al. (Clin. Cancer Res. 5:471-474, 1999) teaches "Although significant progress has been achieved in our understanding of the limitations of gene therapy by suboptimal vectors, host immunological responses to the vectors, and the lack of long term stable expression, the major challenge that limits clinical translation remains in achieving efficient gene delivery to target tissues" (page 474, col. 2, last paragraph).

With respect to using the claimed method for treating a disease, it is noted that the claims encompass treating any disease. Therefore, given the broadest reasonable interpretation

consistent with the specification, the claimed method can be interpreted as treating any disease associated with an abnormally high level of apoptosis such as diabetes by administering a polynucleotide encoding the anti-apoptotic polypeptide to a diabetic patient.

However, regarding gene therapy for diabetes, **Levine** (Mol. Med. Today 5:165-171; 1999) indicates many of the obstacles that need to be overcome in order to create an effective gene therapy for diabetes including gene transfer problems, cell transfer problems, and the responsiveness of the transduced cells to blood glucose levels. Levine focuses on gene transfer into pancreatic beta cells.

Regarding gene transfer into beta cells, Levine indicates that there are two general means by which therapeutic genes can be introduced into beta cells: by transducing the islet cells ex vivo and reintroducing the cells into the pancrease of the subject (see p. 165, last paragraph), and transfer of the therapeutic gene(s) into pancreatic beta-cells in vivo. However, Levine also indicates, "Successful islet cell transplantation has proved to be an elusive goal... (and) to date, there are no studies demonstrating that [in vivo gene transfer into beta-cells] can be done." (See p. 166).

Levine teaches that both type I and type II diabetes results in the apoptotic death of beta-cells (see p. 166-167) and further indicates that preventing beta-cell apoptosis may be potentially applicable to both type I and type II diabetes either by inhibiting apoptosis of beta cells before they die via gene transfer of anti-apoptotic genes such as Bcl-2 into the beta cells (e.g., see p. 168-169). However, gene transfer into beta cells is unpredictable as indicated above.

Furthermore, Levine also indicates that successful gene transfer into beta cells (either in vivo or ex vivo) and/or successful cell transplant are not the only obstacles to obstacle to

overcome in order to effectively treat diabetes. Once the therapeutic gene(s) or cells are successfully delivered, the cells must be able to respond changes in blood glucose levels:

> "A definitive treatment for diabetes mellitus will be one that maintains a normal blood glucose concentration in the face of fluctuating dietary intake. To accomplish this there must be mechanisms to sense the amount of blood glucose coupled to rapid release of the right amount of insulin." (See p. 165, abstract).

Levine summarizes the state of gene therapy for diabetes by stating, "the ultimate goal of a definitive, permanent treatment of diabetes through gene therapy lies in the distant future." (p. 170, last paragraph).

In view of the teachings of Anderson, Deng and Levine, it is clear that gene therapy methods are unpredictable in nature. Furthermore, the specification does not disclose working examples or provide guidance which would overcome the art-recognized problems. Therefore, additional experimentation would be required in order to practice the invention to the full scope encompassed by the claims.

Therefore, in view of the breadth of the claims, the limited amount of direction and/or guidance provided in the specification, as well as the art recognized unpredictability of gene therapy and the limited working examples, it is concluded that an undue amount of experimentation is required for one skilled in the art to make and use the claimed invention to the full scope encompassed by the claims.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 26-28 and 159-161 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. The instant claims are drawn to a transformed cell comprising a nucleic acid of claim 1 or claim 142 wherein the cell can be a mammalian cell including a human cell (e.g., see claims 27, 28, 160 and 161). It is noted that the claims are not limited to an isolated cell. As such, the claims encompass a transformed cell that is present in a human. A non-isolated human cell is non-statutory subject matter. It is noted that amending the claim to an isolated cell that is transformed with the isolated/recombinant nucleic acid of claim 1 would obviate this rejection.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 15, 16, 76, 77, 142- 157 and 159-163 are rejected under 35 U.S.C. 102(b) as being anticipated by Kato et al. (WO 00/00506, previously cited).

Claims 15 encompasses any nucleic acid sequence that hybridizes to SEQ ID NO: 1 under stringent hybridization conditions wherein the nucleic acid is distinct from SEQ ID NO: 37. Claim 16 indicates that the sequence can be 12-10000 base pairs in length. Claims 76 and 77 are drawn to a method of producing a polypeptide that is at least 65% identical to SEQ ID NO: 2 in a cell. Claim 142 encompasses any isolated nucleic acid comprising a polynucleotide

sequence **of** SEQ ID NO: 1 wherein the sequence is distinct from SEQ ID NO: 37 and wherein the [encoded?] polypeptide is an apoptosis inhibitor. Claims 143-148 indicate that the sequence of claim 142 is less than 50kB, 25kB, 10kB, 5kB, 2.5 kB, and from 15 to 2.5 kB in length, respectively. Claims 149-151 indicate that the nucleic acid sequence of claim 142 is attached to a substrate; a plurality of sequences of claim 142 is attached to a substrate wherein the attached sequences are attached at defined positions of a substrate, respectively. Claim 152 encompasses an expression cassette comprising the sequence of claim 142 operably linked to an expression control element, wherein the expression control element is comprises a promoter/enhancer (claim 153), wherein the control element is constitutive, inducible, tissue-specific or developmentally regulated (claim 154), wherein the cassette further comprises a vector (claim 155), wherein the vector confers expression in bacteria, plant, insect, mammal or yeast (claim 156), wherein the vector comprises a viral vector (claim 157). Claims 159-163 encompass a transformed cell comprising the nucleic acid of claim 142, wherein the cell is a bacteria, plant, insect, mammal or yeast cell, wherein the cell is a mammal cell and the mammal is a human, a method for producing a polypeptide comprising expressing the nucleic acid of claim 142 and wherein the nucleic acid is expressed in solution, in a cell in vitro or in vivo, respectively.

It is noted that the limitation "wherein the polypeptide is an apoptosis inhibitor" is a functional limitation. Applicants are reminded that that MPEP 2112.01 indicates:

> "Where the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes, a prima facie case of either anticipation or obviousness has been established. In re Best, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977). 'When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not.'"

Therefore, any sequence that meets the structural limitation of the claim would be identical or substantially identical product and would necessarily have the same function, which in this case is inhibition of apoptosis.

KATO teaches an isolated nucleic acid sequence (see SEQ ID NO: 23 of KATO) that is 1168 nucleotides in length (e.g., see Sequence Listing page 20/45). It is noted that nucleotides 1-700 of KATO's sequence is 100% identical to nucleotide 74-774 of instant SEQ ID NO: 1. SEQ ID NO: 1 is 887 nucleotides in length. Therefore, KATO's sequence comprises a sequence of SEQ ID NO: 1 (specifically nucleotides 74-774 of SEQ ID NO: 1). Furthermore, absent any specific hybridization conditions in the claims, the nucleotide sequence of KATO would hybridize to the sequence set forth as SEQ ID NO: 1 under stringent hybridization conditions because the sequences have 100% identity over 700 contiguous nucleotides. Therefore, the sequence taught by KATO is encompassed by and anticipates claims 15 and 16 because it would hybridize to instant SEQ ID NO: 1 under stringent hybridization conditions and because it is in the range of 1000-2500 nucleotides in length.

Furthermore, KATO's sequence (SEQ ID NO: 23) comprises a polynucleotide sequence of instant SEQ ID NO: 1, specifically, nucleotides 74-774 of SEQ ID NO: 1, and the sequence taught by KATO is 1168 nucleotides in length. Therefore, KATO's sequence meets all of the structural limitations of the nucleic acid of claims 142-163 and must necessarily have the same function (inhibition of apoptosis) (See MPEP 2112.01, as indicated above). KATO also teaches that the sequence can be attached to a "gene chip" or other support (e.g., see p. 12 lines 10-15). It is noted that the specification does not appear to explicitly define the limitation "substrate". As such, the attachment of the nucleic acid to a "gene chip" (as taught by KATO, e.g. page 12)

would constitute attaching the sequence to a substrate. Furthermore, hybridizing a sequence to the nucleic acid sequence (e.g., such as a examining expression patterns—see p. 12) would constitute attaching a plurality of sequences (i.e., a plurality of nucleotides) to a substrate at defined positions. KATO also teaches that the nucleic acid sequence can be comprised in an expression vector such that the vector operably encodes and expresses the polypeptide encoded therein (e.g., see p. 7 lines 2-23). KATO teaches that the expression construct can have a promoter, such as the cytomegalovirus (CMV) promoter (a constitutive promoter) wherein the construct can express the encoded polypeptide in a cell, including a mammalian cell. KATO also teaches the construct can be comprised in a viral vector such as an EBV vector (it is noted that EBV is a herpes virus) (e.g., see p. 7). Furthermore, KATO teaches that the vector can be transformed into cell wherein the cell is a bacterial cell or a eukaryotic cell, including a mammalian cell (e.g., see p. 7, lines 2-23). Therefore, the KATO anticipates claims 142-157 and 159-163.

As indicated above, the sequence of KATO comprises a sequence that is 100% identical to nucleotides 74-774 of instant SEQ ID NO: 1. It appears that the open reading frame of SEQ ID NO: 1 which encodes the 204 amino acid polypeptide of SEQ ID NO: 2 is found at nucleotides 59-671. Therefore, the sequence of KATO comprises nucleotides 74-671 of the open reading frame of SEQ ID NO: 1 and encodes a polypeptide comprising amino acids 16-204 of SEQ ID NO: 2. It is noted that all functional domains disclosed in the instant specification appear to be located in the region between amino acids 16-204 of SEQ ID NO: 1 (e.g., see Figure 1). KATO also teaches that the nucleic acid sequence can be comprised in an expression vector such that the vector operably encodes and expresses the polypeptide encoded therein (e.g., see p.

7 lines 2-23). KATO teaches that the expression construct can have a promoter, such as the cytomeglovirus (CMV) promoter (a constitutive promoter) wherein the construct can express the encoded polypeptide in a cell, including a mammalian cell. KATO also teaches the construct can be comprised in a viral vector such as an EBV vector (it is noted that EBV is a herpes virus) (e.g., see p. 7). Furthermore, KATO teaches that the vector can be transformed into cell wherein the cell is a bacterial cell or a eukaryotic cell, including a mammalian cell (e.g., see p. 7, lines 2-23). Therefore, KATO anticipates claims 76, 77, as well as 142-148, 152-157 and 158-162.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 142, 157 and 158 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kato et al. (WO 00/00506, previously cited) in view of U.S. Patent No. 5,932,210 (Gregory et al.).

As indicated above, KATO teaches an isolated sequence that comprises a sequence that is 100% identical to nucleotides 74-774 of instant SEQ ID NO: 1. It appears that the open reading frame of SEQ ID NO: 1 which encodes the 204 amino acid polypeptide of SEQ ID NO: 2 is found at nucleotides 59-671. Therefore, the sequence of KATO comprises nucleotides 74-671 of the open reading frame of SEQ ID NO: 1 and encodes a polypeptide comprising amino acids 16-204 of SEQ ID NO: 2. Therefore, KATO teaches a nucleotide sequence which encodes a polypeptide that is 92.6% identical to SEQ ID NO: 2 because 189 of the 204 amino acids are the same. KATO also teaches that the nucleic acid sequence can be comprised in an expression vector such that the vector operably encodes and expresses the polypeptide encoded therein in a cell, including a mammalian cell (e.g., see p. 7 lines 2-23). KATO also teaches the construct can be comprised in a viral vector such as an EBV vector (it is noted that EBV is a herpes virus) (e.g., see p. 7). Furthermore, KATO teaches that the vector can be transformed into cell wherein the cell is a bacterial cell or a eukaryotic cell, including a mammalian cell (e.g., see p. 7, lines 2-23).

KATO does not teach that the viral vector is an adenovirus.

Gregory teaches a viral vector that is an adenovirus expression vector that can be used to express a gene of interest in a transformed host cell, such as a mammalian cell.

Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of KATO and Gregory to create an

adenovirus expression vector that encodes as expresses the nucleic acid taught by KATO in a transformed host cell with a reasonable expectation of success.

The motivation to combine the references to create claimed invention is provided by both KATO and Gregory as KATO teaches that it is desirable to express the nucleic acid in a transformed host cell using a viral vector and Gregory teaches a specific adenovirus expression vector that can be used to accomplish the expression of the nucleic acid in a transformed host cell.

Claim Objections

Claims 24 and 24 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Response to Arguments

Applicant's arguments filed 12/12/2005 have been fully considered by the Examiner.

With respect to the rejection of claims under 35 USC 112, 2nd paragraph, the amendment and/or arguments render the rejection of record moot, however, a new grounds of rejection under 35 USC 112, 2nd paragraph has been set forth for the reasons indicated herein.

With respect to the rejection of claims under 35 USC 112, 1st paragraph (New Matter), the amendment and/or arguments render the rejection of record moot.

With respect to the rejection of claims under 35 USC 112, 1st paragraph (Written Description) Applicants argue that they have identified and discussed specific functional

domains of the polypeptide of SEQ ID NO: 2 including the BH1 domain, BH2 domain, BH3 domain, BH4 domain, transmembrane domain and dimerization domain as well as Bcl-B mutants. However, applicants arguments are not persuasive because the claims that are rejected herein for insufficient written description do not indicate that the sequences of the instant claims posses any particular function, as such the claims encompass sequences which have the required level of sequence identity but which may have completely different functions or which may be non-functional. Therefore, Applicants arguments are not persuasive.

With respect to the rejection of claims under 35 USC 112,1st paragraph (enablement) applicants arguments have been fully considered and the arguments and/or amendment is sufficient to overcome the rejection of record. However a new grounds of rejection under 35 USC 112, 1st paragraph has been set forth herein for the reasons indicated above.

With respect to the rejection of claims under 35 USC 102, Applicants argue that the Examiner acknowledges, "the sequence disclosed by KATO is not the sequence of the current polynucleotides" (Emphasis is by Applicants). In response, it is acknowledged that the sequence disclosed by KATO is not the sequence that is SEQ ID NO: 1. However, the instant claims are not limited to the sequence that is SEQ ID NO: 1. Furthermore, as indicated herein, KATO does teach a sequence that comprises all of the structural limitations set forth in the claims.

Applicants argue that the Examiner's reasoning equates to rejecting all polynucleotide sequences having an ATG start codon because at that level one can find 100% identity. In response, it is respectfully pointed out that what Applicants assert is a different fact pattern than is present here. KATO does not merely teach that comprises a sequence that 100% identical to a sequence of SEQ ID NO: 1, KATO teaches a sequence that comprises 100% identity to 700

contiguous nucleotides of SEQ ID NO: 1 and which encodes a polypeptide that is 100% identical to amino acids 16-204 of SEQ ID NO: 2. Furthermore, the sequence taught by KATO meets all of the structural limitations of the claims. It is respectfully pointed out that limiting the claims to a nucleotide sequence which encodes the polypeptide that is SEQ ID NO: 2 would obviate the instant rejection. However, the instant claims are not so limited and encompass any nucleic acid sequence that hybridizes to the sequence set forth as SEQ ID NO: 1 under stringent conditions wherein the sequence is distinct from SEQ ID NO: 37 (claim 15); a method of expressing a nucleic acid that encodes a protein that is at least 65% identical to SEQ ID NO: 2 (claim 76), as well as a nucleic acid comprising a polynucleotide sequence of SEQ ID NO: 1 wherein the sequence is distinct from SEQ ID NO: 37 and wherein the polypeptide is an apoptosis inhibitor (claim 142). Therefore, KATO teaches an isolated nucleic acid which meets all of the structural limitations of the claims and thus anticipate the indicated claims.

Applicants summarize the general teaching of KATO, which the Examiner does not take issue with other than to point out that KATO specifically teaches a polynucleotide that meets all of the structural limitations of the claims.

Applicants argue that SEQ ID NO: 23 of KATO does not teach residues 1-887 of the claimed polynucleotide and that the structure of KATO's SEQ ID NO: 23 is substantially from the Applicants sequence. These arguments are not persuasive because the claims are not limited to a sequence that comprises residues 1-887 of SEQ ID NO: 1. As indicated above, KATO teaches a sequence that meets all of the structural limitations of the claims. Furthermore, as indicated above, MPEP 2112.01 indicates:

> "Where the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes,

> a prima facie case of either anticipation or obviousness has been established. In re Best, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977). 'When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not.'"

Therefore, any sequence that meets the structural limitation of the claim would be identical or substantially identical product and would necessarily have the same function.

With respect to the "sense and antisense probes" arguments, it is respectfully pointed out that the instant rejection does not rely on "DNA fragments" of SEQ ID NO: 23, as argued by Applicants. The instant rejection relies on the teaching of the entire sequence of SEQ ID NO: 23 by KATO which comprises a sequence that is 100% identical to nucleotides 74-774 (out of a total of 887 nucleotides) of instant SEQ ID NO: 1. Thus KATO teaches a sequence which meets all of the structural limitations of the claims. Therefore, Applicants arguments are not persuasive.

With respect to the "gene chip and recombinant system" arguments, Applicants argue that KATO cannot anticipate the claims because KATO fails to teach the current polynucleotide sequence. The Examiner respectfully disagrees because as indicated above, KATO teaches a sequence which meets all of the structural limitations of the instant claims. Therefore, Applicants arguments are not persuasive.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jon Eric Angell whose telephone number is 571-272-0756. The examiner can normally be reached on Mon-Fri, with every other Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

J.E. Angell, Ph.D.
Patent Examiner
Art Unit 1635

JON ANGELL
PATENT EXAMINER